

What is claimed is:

1. A method for radiolabeling thiol-containing peptides with fluorine-18 (^{18}F -18), comprising reacting a peptide comprising a free thiol group with a labelling reagent having the general formula $^{18}\text{F}-(\text{CH}_2)_m-\text{CR}_1\text{R}_2-(\text{CH}_2)_n-\text{X}$, wherein:

n is 0, 1 or 2;

m is 0, 1 or 2;

and $n+m$ is 0, 1, or 2;

X is selected from the group consisting of iodide, bromide, chloride, azide, tosylate, mesylate, nosylate, triflate, unsubstituted maleimide, maleimide substituted with one or two alkyl groups, and 3-sulfo-maleimide; and

R_1 and R_2 are the same or different and are selected from the group consisting of iodide, bromide, chloride, azide, tosylate, mesylate, nosylate, triflate, hydrogen, $-\text{CONH}_2$, carboxyl, hydroxyl, sulfonic acid, tertiary amine, quaternary ammonium, unsubstituted alkyl, substituted alkyl, $-\text{COOR}'$, $-\text{CONR}'_2$, or COR' , wherein the substituents of the substituted alkyl groups are selected from the group consisting of $-\text{CONH}_2$, carboxyl, hydroxyl, sulfonic acid, tertiary amine and quaternary ammonium and wherein R' is a C_1 - C_6 alkyl or phenyl.

2. The method according to claim 1, wherein X is I and at least one of R_1 and R_2 is I.

3. The method according to claim 1, wherein the peptide is selected from the group consisting of $\text{F}(\text{ab}')_2$, $\text{F}(\text{ab})_2$, Fab' and Fab antibody fragments, single-chain antibody subfragments, divalent antibody fragment constructs, and antibody constructs comprising IgG_3 or $\text{IgG}_3\text{-F}(\text{ab}')_2$ frameworks.

4. The method according to claim 1, wherein the labelling reagent is selected from the group consisting of $^{18}\text{F}-\text{Cl}_3$, $^{18}\text{F}-\text{CHCl}_2$, $^{18}\text{F}-\text{CHICOOCH}_3$, $^{18}\text{F}-\text{Cl}_2\text{COOH}$, $^{18}\text{F}-\text{Cl}_2\text{COOCH}_3$, $^{18}\text{F}-\text{Cl}_2\text{CH}_2\text{OH}$, $^{18}\text{F}-\text{CHICH}_2\text{OH}$, $^{18}\text{F}-\text{Cl}_2\text{CH}_2\text{COOH}$, $^{18}\text{F}-\text{Cl}_2\text{CH}_2\text{N}^+(\text{CH}_3)_3$, $^{18}\text{F}-\text{I}_2\text{CH}_2\text{-maleimide}$, $^{18}\text{F}-\text{CHICONH}_2$, $^{18}\text{F}-\text{Cl}_2\text{CONH}_2$, $^{18}\text{F}-\text{CHICO}_2\text{CH}_3$, $^{18}\text{F}-\text{Cl}_2\text{CO}_2\text{CH}_3$, $^{18}\text{F}-\text{CHBr}_2$, $^{18}\text{F}-\text{CBr}_2\text{CH}_2\text{CH}_2\text{-SO}_3\text{H}$, $^{18}\text{F}-\text{CBr}_2\text{CH}_2\text{OH}$,

$\text{CF}_3\text{COCl}_2\text{-}^{18}\text{F}$, $\text{CH}_3\text{COCBr}_2\text{-}^{18}\text{F}$, $^{18}\text{F-CHBrCN}$, $^{18}\text{F-Cl}_2\text{CHCN}$, $\text{CBrF}_2\text{-}^{18}\text{F}$ and $^{18}\text{F-CBr}(\text{CONH}_2)_2$.

5. The method according to claim 1, wherein the labelling reagent is selected from the group consisting of $^{18}\text{F-CH}_2\text{Cl}_2\text{COOH}$ and $^{18}\text{F-CH}_2\text{Cl}_2\text{CONH}_2$.

6. A method for radiolabeling thiol-containing peptides with fluorine-18 (F-18), comprising reacting a peptide comprising a free thiol group with a F-18 fluorinated alkene, wherein at least one of the two double-bonded carbon atoms bears at least one leaving group selected from the group consisting of iodide, bromide, chloride, azide, tosylate, mesylate, nosylate and triflate.

7. The method of claim 6, wherein the F-18 fluorinated alkene is selected from the group consisting of $^{18}\text{F-CH=Cl}_2$, $^{18}\text{F-CI=CH}_2$, and $^{18}\text{F-CI=Cl}_2$.

8. The method according to claim 6, wherein the peptide is selected from the group consisting of F(ab')_2 , F(ab)_2 , Fab' and Fab antibody fragments, single-chain antibody subfragments, divalent antibody fragment constructs, and antibody constructs comprising IgG_3 or $\text{IgG}_3\text{-F(ab')}_2$ frameworks.

9. A method for detecting a tissue comprising:

(a) administering to a patient a bispecific antibody or antibody fragment comprising an arm that is specific to a target tissue of the patient and another arm that is specific to an F-18-labeled peptide or a low molecular weight hapten conjugated to the F-18-labeled peptide; and allowing the bispecific antibody or antibody fragment to bind to the target tissue, and the non-targeted bispecific antibody or antibody fragment to clear;

(b) administering the F-18-labeled peptide or the hapten conjugate thereof to the patient, and allowing the F-18-labeled peptide or the hapten conjugate thereof to bind to the bispecific antibody or the antibody fragment, and the unbound F-18-labeled peptide or hapten conjugate thereof to clear; and

(c) detecting the F-18-labeled peptide, thereby detecting the target tissue.

10. The method according to claim 9, wherein the F-18-labeled peptide contains a thiol group.

11. The method according to claim 10, wherein the F-18-labeled peptide is labeled by the method according to claim 1.

12. The method according to claim 10, wherein the F-18-labeled peptide is labeled by the method according to claim 6.

13. The method according to claim 9, wherein the F-18-labeled peptide is X-Gly-D-Tyr-D-Trp-Gly-D-Lys(X)-Gly-D-Tyr-D-Trp-OH, and X represents a free or protected amino acid group.

14. The method according to claim 9, wherein the F-18-labeled peptide is Ac-Cys(Y)-D-Tyr-D-Trp-Gly-D-Cys(Y)-Gly-D-Tyr-D-Trp-OH, and Y represents a free or protected thiol group.

15. The method according to claim 9, wherein the F-18-labeled peptide is Ac-Gly-D-iodo-Tyr-D-Trp-Gly-D-Lys(Ac)-Gly-D-iodo-Tyr-D-Trp-OH.

16. The method according to claim 9, wherein the hapten is a metal chelate complex.

17. The method according to claim 16, wherein the metal chelate complex comprises manganese, iron, or gadolinium.

18. The method according to claim 9, wherein the bispecific antibody or antibody fragment is monoclonal.

19. The method according to claim 9, wherein the antibody or antibody fragment is humanized.

20. The method according to claim 9, wherein the F-18-labeled peptide is detected by positron emission tomography.